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## Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the present application.

### Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1. (currently amended) A compound of structural formula I:

$$R^3$$
 $R^2$ 
 $N$ 
 $R^1$ 

or a pharmaceutically acceptable salt thereof, wherein:

R I is calasted for

Kr is selected from:
——————————————————————————————————————
<del></del>
$\frac{\text{(3)}  \text{NReRb}_{i}}{\text{NReRb}_{i}}$
(4)NR <sup>b</sup> C(O)Ra,
<del>- (5) CO2Ra,</del>
——————————————————————————————————————
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<del>(8) SO2Rb,</del>
(1) <u>C<sub>1-6</sub>alkyl</u> ,
(2) _OH

- (3) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (4) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (5) cycloalkyl-C1-4alkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (6) cycloheteroalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (7) cycloheteroalkyl-C1\_4 alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (8) phenyloxy, unsubstituted or substituted with one to three R<sup>o</sup> substituents,
- (9) heteroaryloxy, unsubstituted or substituted with one to three Rc substituents,
- (10) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three Rc substituents,

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- (11) heteroaryl-C<sub>1-4</sub>alkyloxy, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (12) -NRaRb.
- (13) -NRbC(O)Ra.
- (14) -CO<sub>2</sub>H,
- (15) C<sub>1-6</sub>alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (16) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyl-C<sub>1-4</sub>alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (19) heteroaryloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) phenyl-C<sub>1</sub>\_4alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (21) heteroaryl-C<sub>1</sub>-4alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (22) -C(O)NRaRb.
- (23) cyano,
- (24) -SO<sub>2</sub>C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents; and provided that R<sup>1</sup> is not -NH<sub>2</sub>;

### R<sup>2</sup> is selected from:

- (1) hydrogen,
- (2)  $C_{1-10}$ alkyl,
- (3) -ORa,
- (4) -NRaRb.
- (5) -NRaC(O)Rb,
- (6) -CQ2Ra,
- (7) -C(O)NRaRb,
- (8) cyano,
- (9) -SRa, and
- (10)  $-SO_2R^2$ ;

wherein R<sup>3</sup> and R<sup>4</sup> are each independently selected from:

each Ra is independently selected from:

- (1) hydrogen,
- (2) C<sub>1-10</sub>alkyl,
- (3) C2-10 alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C<sub>1-10</sub>alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C<sub>I-10</sub> alkyl;
- (8) aryl,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl; and

each  $R^{\mbox{\scriptsize b}}$  is independently selected from:

- (1) hydrogen,
- (2)  $C_{1-10}$ alkyl,
- (3) C2-10 alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C<sub>1-10</sub>alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C<sub>1-10</sub> alkyl;
- (8) aryl,

- (9) heteroaryl,
- (10) aryi-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl, or

R<sup>a</sup> and R<sup>b</sup> together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R<sup>d</sup>,

each Ra and Rb may be unsubstituted or substituted with one to three substituents selected from Rc; each Rc is independently selected from:

- (1) C<sub>1-10</sub>alkyl,
- (2) -ORd,
- (3)  $-NReS(Q)_mRd$
- (4) halogen,
- (5) -SRd,
- (6)  $-S(O)_mNRdRe$ ,
- (7) -NRdRe,
- (8) -C(O)Rd
- (9) -CO<sub>2</sub>Rd,
- (10) -CN,
- (11) -C(O)NRdRe,
- (12) -NReC(O)Rd,
- (13) -NRCC(O)ORde,
- (14) -NReC(O)NRdRe,
- (15) -CF3,
- (16) -OCF3,
- (17) cycloheteroalkyl,
- (18) aryl,
- (19) arylC<sub>1</sub>.4alkyl,
- (20) heteroaryl, and
- (21) heteroaryiC1.4alkyl;

Rd and Re are independently selected from:

- (1) hydrogen,
- (2) C<sub>1-10</sub>alkyl,
- (3)  $C_{2-10}$  alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl;
- (6) cycloheteroalkyl,

- (7) cycloheteroalkyl-C<sub>1-10</sub> alkyl;
- (8) aryl,
- (9) heteroaryl,
- (10) aryi-C1-10alkyi, and
- (11) heteroaryl-C1-10alkyl, or

Rd and Re together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rf,

each  $R^d$  and  $R^c$  may be unsubstituted or substituted with one to three substituents selected from  $R^f$ ;  $R^f$  is independently selected from:

- (1) halogen,
- (2) C<sub>1-10</sub>alkyl,
- (3) -O-C<sub>1-4</sub>alkyl,
- (4) -S-C1-4alkyl,
- (5) -CN,
- (6) -CF3, and
- (7) -OCF3;

each Rg is independently selected from:

- (1) halogen,
- (2) C<sub>1-10</sub>alkyl,
- (3) -O-C1-4alkyl,
- (4) -S-C<sub>1-4</sub>alkyl,
- (5) -CN,
- (6) -CF3, and
- (7) -OCF3; and

m is selected from 1 and 2.

Claim 2. (canceled)

Claim 3. (canceled)

Claim 4. (currently amended) The compound according to Claim 1, wherein:

## R+ is selected from:

- (1) C1 6alkyl,
- (2) OH,
- (3) OC1-6alkyl, unsubstituted or substituted with one to three Ro substituents,

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- (4) cycloalkyloxy, unsubstituted or substituted with one to three R6 substituents,
- (5) cycloalkyl-61\_4alkyloxy , unsubstituted or substituted with one to three R<sup>6</sup> substituents,
- (6) cycloheteroalkyloxy, unsubstituted or substituted with one to three Ro substituents,
- (7)—eyelohoteroalkyl C<sub>1</sub> 4 alkyloxy, unsubstituted or substituted with one to three Resubstituents,
- (8) phenyloxy, unsubstituted or substituted with one to three Ro substituents,
- (9) heteroaryloxy, unsubstituted or substituted with one to three R6 substituents,
- (10) phenyl-G1\_4alkyloxy, unsubstituted or substituted with one to three R6 substituents.
- (11)—heteroaryl C<sub>1</sub>\_4alkyloxy, unsubstituted or substituted with one to three Ro substituents.
- (12) NRaRb.
- (13) NR<sup>b</sup>C(O)Ra.
- (14) CO2H.
- (15) C1\_6alkyloxycarbonyl, unsubstituted or substituted with one to three R0 substituents,
- (16) cycloalkyloxycarbonyl, unsubstituted or substituted with one to three R6 substituents.
- (17)—cycloalkyl-G<sub>1</sub>.4alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three Re substituents,
- (19) heteroaryloxyearbonyl, unsubstituted or substituted with one to three R6 substituents,
- (20) phenyl-C1 4alkyloxycarbonyl, unsubstituted or substituted with one to three Resubstituents.
- (21) heteroaryl-G<sub>1.4</sub>alkyloxyearbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents:
- (22) C(O)NR2Rb,
- (23) cyano,
- (24) SO<sub>2</sub>G<sub>1-6alkyl, unsubstituted or substituted with one-te-three Re-substituents; and Ra and Rb are each selected from:</sub>
  - (1) hydrogen,
  - (2) C1-6alkyl, unsubstituted or substituted with one to three RC substituents,
  - (3) cycloalkyl, unsubstituted or substituted with one to three Rc substituents,
  - (4) cycloalkyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents,
  - (5) phenyl, unsubstituted or substituted with one to three Rc substituents,
  - (6) heteroaryl, unsubstituted or substituted with one to three RC substituents,
  - (7) phenyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents, or

(8) heteroaryl-C<sub>1</sub>-4alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or when bonded to nitrogen, R<sup>a</sup> and R<sup>b</sup> together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to three R<sup>c</sup> substitutents;

or a pharmaceutically acceptable salts thereof.

Claim 5. (currently amended) The compound according to Claim 4, wherein R1 is selected from:

- (1) (1) C<sub>1</sub>-6alkyl,
- (2) OH,
- (3) (2) OC1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (4) (3) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two Rc substituents.
- (5) (4) cycloalkyl-C<sub>1-3</sub>alkyloxy-, unsubstituted or substituted with one to two Rc substituents,
- (6) (5) phenyloxy, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (7) (6) pyridyloxy, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (8) (7) phenyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
- (9) (8) pyridyl-C<sub>1-3</sub>alkyloxy, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (10) (9)\_-NRaRb, wherein:

## Ra is selected from:

- (a) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three Rc substituents,
- (b) cycloalkyl, unsubstituted or substituted with one to two Rc substituents,
- (c) cycloalkyl-C<sub>1</sub>\_4alkyl, unsubstituted or substituted with one to two Rc substituents,
- (d) phenyl, unsubstituted or substituted with one to two Rc substituents,
- (e) heteroaryl, unsubstituted or substituted with one to two Rc substituents,
- (f) benzyl, unsubstituted or substituted with one to two  $R^c$  substituents,  $R^b$  is selected from:
- (a) hydrogen,
- (b) C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or R<sup>a</sup> and R<sup>b</sup> together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to two R<sup>c</sup> substitutents,

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## (11) (10) -NRbC(O)Ra, wherein:

#### Ra is selected from:

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two Rc substituents,
- (d) cycloalkyl-C<sub>1</sub>-4alkyl, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (e) phenyl, unsubstituted or substituted with one to two RC substituents,
- (f) pyridyl, unsubstituted or substituted with one to three Rc substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,
- (h) pyridylmethyl-, unsubstituted or substituted with one to three Rc substituents,

## Rb is selected from:

- (a) hydrogen,
- (b) C<sub>1-6alkyl</sub>, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (12) (11) -CO<sub>2</sub>H,
- (13) (12) C<sub>1</sub>-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (14) (13) -C(O)NRaRb, wherein:

## Ra is selected from:

- (a) hydrogen,
- (b) C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, R<sup>b</sup> is selected from:
- (a) hydrogen, and
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (15) (14) cyano
- (16) (15) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (17) (16) -SO<sub>2</sub>C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents; each R<sup>c</sup> is independently selected from:

## (1) C<sub>1-3</sub>alkyl,

- (2) hydroxy,
- (3) -OC<sub>1-3</sub>alkyl,
- (4) halogen,
- (5) -SCH<sub>3</sub>,
- (6) -SH,
- (7) -NRdRe.
- (8) -C(0)C<sub>1-3</sub>alkyi

- (9) -CO<sub>2</sub>C<sub>1-3</sub>alkyl,
- (10) -CO<sub>2</sub>H,
- (11) -CN,
- (12) -CF<sub>3</sub>,
- (13) -OCF3,
- (14) cycloheteroalkyl,
- (15) phenyl,
- (16) benzyl, and
- (17) pyridyl;

or a pharmaceutically acceptable salts thereof.

Claim 6. (previously presented) The compound according to Claim 4, wherein R2 is selected from:

- (1) hydrogen,
- (2) C<sub>1-6</sub>alkyl,
- (3) -OH,
- (4) -OC1-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (5) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (6) cycloalkyl-C<sub>1</sub>-4alkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (7) cycloheteroalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (8) cycloheteroalkyl-C<sub>1-4</sub> alkyloxy, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (9) phenyloxy, unsubstituted or substituted with one to three Rc substituents,
- (10) heteroaryloxy, unsubstituted or substituted with one to three Rc substituents,
- (11) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (12) heteroaryl-C<sub>1</sub>-4alkyloxy, unsubstituted or substituted with one to three Rc substituents,
- (13) -NRaRb.
- (14) -NRbC(Q)Ra,
- (15) -CO<sub>2</sub>H,
- (16) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents.
- (18) cycloalkyl-C<sub>1-4</sub>alkyloxycarbonyl-, unsubstituted or substituted with one to three R¢ substituents,

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- (19) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) heteroaryloxycarbonyl, unsubstituted or substituted with one to three R¢ substituents,
- (21) phenyl-C<sub>1-4</sub>alkyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (22) heteroaryl-C<sub>1</sub>-4alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (23) -C(O)NRaRb,
- (24) cyano,
- (25) -SC1-6alkyl, unsubstituted or substituted with one to three RC substituents, and
- (26) -SO<sub>2</sub>C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or a pharmaceutically acceptable salts thereof.

Claim 7. (previously presented) The compound according to Claim 1, wherein: R<sup>2</sup> is selected from:

- (1) hydrogen,
  - (2) C1-6alkyl,
  - (3) -OH,
  - (4) -OC1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
  - (5) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
  - (6) C4-7cycloalkyl-C1-3alkyloxy-, unsubstituted or substituted with one to two Rc substituents,
  - (7) phenyloxy, unsubstituted or substituted with one to two Rc substituents,
  - (8) pyridyloxy, unsubstituted or substituted with one to two Rc substituents,
  - (9) phenyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
  - (10) pyridyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
  - (11) -NRaRb, wherein:

### Ra is selected from:

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three Rc substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two RC substituents,
- (d) cycloalkyl-C<sub>1</sub>-4alkyl, unsubstituted or substituted with one to two RC substituents,
- (e) phenyl, unsubstituted or substituted with one to two RC substituents,
- (f) heteroaryl, unsubstituted or substituted with one to two RC substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,

Rb is selected from:

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or R<sup>a</sup> and R<sup>b</sup> together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members, unsubstituted or substituted on carbon with one to two R<sup>c</sup> substitutents.
- (12) -NHC(O)Ra, wherein:

Ra is selected from:

- (a) hydrogen,
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- cycloalkyl-C<sub>1-4</sub>alkyl, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (e) phenyl, unsubstituted or substituted with one to two Rc substituents,
- (f) pyridyl, unsubstituted or substituted with one to three Rc substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,
- (h) pyridylmethyl-, unsubstituted or substituted with one to three RC substituents.
- (13) cyano, and
- (14) -SO<sub>2</sub>C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents; or a pharmaceutically acceptable salts thereof.

Claim 8. (currently amended) The compound according to Claim 1, wherein: R1 is selected from:

- (1) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- ——(2) OH
  - (3) (2) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
  - (4)(3) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
  - $\frac{(5)(4)}{(5)}$  cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
  - (6)(5) 4-fluorophenyloxy, 4-chlorophenyloxy, 4-methoxyphenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy,

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(7) (6) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,

(8)(7) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 2,4-dichlorobenzyloxy, alpha-methyl-4-fluorobenzyloxy, alpha-methyl-4-chlorobenzyloxy, alpha-dimethyl-4-fluorobenzyloxy, or alpha-alpha-dimethyl-4-chlorobenzyloxy,

(9)(8) 2-pyridylmethyloxy 3,-pyridylmethyloxy, or 4-pyridylmethyloxy,
(10)(9) N-methylamino, N,N-dimethyamino, N,N-diisopropylamino, or
N(CH3)CH2CH2N(CH3)2, or N-containing heterocycloalkyl bonded via nitrogen selected

from: morpholinyl, thiomorpholinyl, <u>pyrrolidinyl</u>, piperidinyl, and [2.2.1]azabicycloheptyl, (11)(10) -NHCOR<sup>a</sup> wherein R<sup>a</sup> is selected from:

- (a) hydrogen,
- (b) C<sub>1-4</sub>alkyl,
- (c) C4-6cycloalkyl, and
- (d) phenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, or 3,4-

### dichlorophenyl,

(12)(11) -CO<sub>2</sub>H, (13)(12) -C(O)NH<sub>2</sub>, (14)(13) -CN, and (15)(14) -SO<sub>2</sub>CH<sub>3</sub>:

### R2 is selected from:

- (1) hydrogen,
- (2) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- (3) -OH,
- (4) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (5) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (6) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (7) 4-fluorophenyloxy, 4-chlorophenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3-chlorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, or phenyloxy,

- (8) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 2,4-fluorobenzyloxy, or 2,4-dichlorobenzyloxy,
- (9) 4-pyridyloxy, 3-pyridyloxy, 2-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (10) amino, N-methylamino, N-ethylamino, N,N-dimethyamino, N,N-diethylamino,N,N-disopropylamino, or N-containing heterocycloalkyl bonded via nitrogen selected from: pyrrolidinyl, and piperidinyl,
- (11) -NHCORa wherein Ra is selected from:
  - (a) hydrogen, and
  - (b) C<sub>1-4alkyl</sub>,
- (12) -CN, and
- (13)  $-SO_2CH_3$ ;

R3 and R4 are each independently selected from:

- (1) 4-chlorophenyl,
- (2) 4-methoxyphenyl,
- (3) 4-fluorophenyl,
- (4) 4-trifluoromethylphenyl,
- (5) 3-chlorophenyl,
- (6) 3-methoxyphenyl,
- (7) 2,4-dichlorophenyl, and
- (8) 2-chloro-4-methylthiophenyl;

or a pharmaceutically acceptable salts thereof.

Claim 9. (previously presented) The compound according to Claim 8, wherein:

R<sup>3</sup> is 4-chlorophenyl and R<sup>4</sup> is 2,4-dichlorophenyl, or a pharmaceutically acceptable salt thereof.

Claim 10 (canceled)

Claim 11. (currently amended) A method of treating a disease mediated by the Cannabinoid-1 receptor selected from: psychosis, memory deficit, cognitive disorders, migraine, neuropathy, neuro-inflammatory-disorders, corebral vascular accidents, head-trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, sohizophrenia, substance abuse disorders, constipation, chronic intestinal pseudo-obstruction, citrhosis of the liver, asthma, obesity, and other cating disorders associated with excessive food intake, comprising administration to a patient in need of such

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treatment of a therapeutically effective amount of a compound according to Gleim 1 compound of structural formula I:

$$R^3$$
 $R^4$ 
 $R^2$ 
 $N$ 
 $R^1$ 

**(I)** 

or a pharmaceutically acceptable salt thereof, wherein:

## R1 is selected from:

- (1) C1-10alkyl,
  - (2) -ORa,
- (3) -NRaRb
- -NRbC(O)Ra. (4)
- <u>(5)</u> -CO2Ra.
- (6) -C(O)NRaRb
- (7) cyano, and
- (8) -SO2Rb

# provided that R1 is not -NH2:

## R2 is selected from:

- (1) hydrogen,
- (2) C1-10alkyl.
- (3) -ORa.
- <u>(4)</u> -NRaRb
- <u>(5)</u> -NRaC(O)Rb,
- <u>(6)</u> -CO2Ra,
- <u>(7)</u> -C(O)NRaRb.
- <u>(8)</u> cyano,
- (2) -SRa, and
- (10) -SO<sub>2</sub>Ra;

# wherein R3 and R4 are each independently selected from:

<u>(I)</u>

$$R_a$$

(3)

(4) \_\_\_\_\_\_\_R<sup>g</sup>

# each Ra is independently selected from:

- (I) hydrogen,
- (2) C1-10alkyl.
- (3) C2-10 alkenyl.
- (4) cycloalkyl.
- (5) cycloalkyl-C1-10alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C1-10 alkyl;
- (8) aryl,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl; and

# each Rb is independently selected from:

- (1) hydrogen,
- (2) <u>C<sub>1-10</sub>alkyl</u>,
- (3) <u>C2-10 alkenyl</u>,
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl:
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyi-C1-10 alkyi;
- (8) aryl,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl, or

Ra and Rb together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd.

each Ra and Rb may be unsubstituted or substituted with one to three substituents selected from Rc; each Rc is independently selected from:

- (1)  $C_{1-10}$ alkyl,
- (2) -ORd,
- $(3) -NReS(O)_mRd,$
- (4) halogen,
- (5) -SRd.
- (6) -S(O)mNRdRe
- (7) -NRdRe.
- (8) -C(O)Rd
- (9) <u>-CO<sub>2</sub>Rd</u>
- (10) -CN,
- (11) -C(O)NRdRe.
- (12) -NReC(O)Rd,
- (13) -NRC(O)ORde,
- (14) -NRC(O)NRdRe,
- (15) -CF3,
- (16) -OCF3,
- (17) cycloheteroalkyl.
- (18) aryl,
- (19) arylC<sub>1</sub> 4alkyl,
- (20) heteroaryl, and
- (21) heteroaryiC<sub>1-4alkyl</sub>;

# Rd and Re are independently selected from:

- (1) hydrogen.
- (2) C1-10alkyl.
- (3) C2-10 alkenyl.
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl:
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C1-10 alkyl:
- (8) aryl,
- (9) heteroaryl,

(10) aryl-C1-10alkyl, and

(11) heteroaryl-C1-10alkyl, or

Rd and Re together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rf.

each Rd and Re may be unsubstituted or substituted with one to three substituents selected from Rf. Rf is independently selected from:

- (1) halogen,
- (2) <u>C</u>1-10alkyl,
- (3) -O-C<sub>1</sub>-4alkyl,
- (4) -S-C<sub>1-48lkyl</sub>
- (5) -CN,
- (6) <u>-CF3</u>, and
- (7) -OCF3;

## each Rg is independently selected from:

- (1) halogen,
- (2) <u>C<sub>1-10alkyl</u>,</u></sub>
- (3) <u>-O-C</u><sub>1-42lkyl.</sub>
- (4) <u>-S-C1-4alkyl.</u>
- (5) -CN.
- (6) -CF3, and
- (7) -OCF3; and

## m is selected from 1 and 2.

Claim 12. (canceled)

Claim 13. (previously presented)

The method according to Claim 11 wherein the disease mediated by the Cannabinoid-1 receptor is an eating disorder associated with excessive food intake.

Claim 14. (currently amended) The method according to Claim 13 wherein the cating disorder associated associated with excessive food intake is selected from obesity, bulimia nervosa, and compulsive eating disorders.

Claim 15. (original) The method according to Claim 14 wherein the eating disorder associated with excessive food intake is obesity.

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#### Claim 16. (cancelled)

Claim 17. (original) A composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.

Claims 18-24 (cancelled)

Claim 25. (currently amended) The method according to Claim 11 for treating substance abuse disorders, wherein the abused substance is nicotine in a person dependent on nicotine; comprising administering a therapeutically effective amount of a compound according to Claim 1 to the person.

Claim 26. (new) The compound according to Claim 1, selected from:

- (1) 2-(4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (2) 2-(4-fluorobenzyloxy)-4-(2-chloro-4-methylthiophenyl)-5-(4-chlorophenyl)-pyrimidine;
- (3) 2-(3,4-difluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (4) 2-(3,4-difluorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (5) 2-(4-chlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (6) 2-(4-chlorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (7) 2-(3,4-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (8) 2-(3,4-dichlorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (9) 2-(3-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (10) 2-(3-fluorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (11) 2-(3-chlorobenzylamino)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-pyrimidine;
- (12) 2-(N,N-dimethylamino)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (13) 2-carboxy-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (14) 2-methoxy-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (15) 2-(3,4-difluorobenzyloxy)-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (16) 2-(3,4-difluorobenyloxy)-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (17) 2,4-bis-(3,4-difluorobenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (18) 2,4-dimethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (19) 2,4-dicthoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (20) 2,4-diisopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (21) 2-methylsulfonyl-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (22) 2,4-bis(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (23) 2-cyano-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (24) 2-(3,4-difluorobenzyloxy)-4-cyano-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (25) 2-cyano-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (26) 2,4-bis(cyano)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (27) 2-(3,4-difluorophenoxy)-4-methyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (28) 2-ethyl-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (29) 2-isopropy-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (30) 2-(3,4-difluorobenzyloxy)-4-methyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (31) 2-(3,4-difluorobenzyloxy)-4-ethyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (32) 2-(3,4-difluorobenzyloxy)-4-(N-methylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (33) 2-(3,4-difluorophenoxy)-4-amino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (34) 2-(3,4-difluorobenzyloxy)-4-(amino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (35) 2-(3,4-difluorophenoxy)-4-(acetylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (36) 2-(3,4-difluorobenzyloxy)-4-(acetylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (37) 2-(3,4-difluorophenoxy)-4-(N-pytrolidinyl)-5-[4-chlorophenyl]-6-[2,4-dichlorophenyl]
- (38) 2-(cyclopropylmethoxy)-4-(N-pyrrolidinyl)-5-[4-chlorophenyl]-6-[2,4-dichlorophenyl] pyrimidine;
- (39) 2-(N,N-diethylamino)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (40) 2-(N,N-diisopropylamino)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (41) 2-(N-pyrrolidinyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (42) 2-(N-piperidyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (43) 2-(N-morpholinyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (44) 2-(7-N-[2.2.1]-azabicycloheptyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (45) 2-(n-propionyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (46) 2-(N-(2-methyl)propionyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (47) 2-(N-(3-methyl)butyryl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (48) 2-(aminocarbonyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (49) 2-(carboxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (50) 2-(2-hydroxyethyleneoxy)-4-(3,4-difluorophcnoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (51) 2-(2-methoxyethyleneoxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (52) 2-(cyclohexylmethyloxy)-4-isopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (53) 2-cyclohexyloxy-4-isopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (54) 2-(3,4-difluorophenoxy)-4-cyclohexyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (55) 2-(3,4-diffuorobenzyloxy)-4-cyclohexyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (56) 2,4-bis(cyclopropylmethyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (57) 2-cyclopropyloxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (58) 2-(N-pyrrolidinyl)-4-cyclopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (59) 2,4-bis(isopropyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (60) 2-(3,4-difluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (61) 2-(4-chlorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (62) 2-(3-fluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (63) 2-(3-chlorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (64) 2-(4-fluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (65) 2-(α-methyl-4-fluorobenzyloxy-)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (66) 2-(α-methyl-4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (67) 2-(3-pyridylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (68) 2-(n-butyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (69) 2-(2,4-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (70) 2-(cyclohexylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (71) 2-(3,5-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (72) 2-(6-chloro-3-pyridylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (73) 2-(α,α-dimethyl-4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (74) 2-(4-fluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;

- (75) 2-(3-fluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (76) 2-(3,4-difluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (77) 2-(3-chlorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (78) 2-(4-methoxyphenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (79) 2-(3-pyridyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (80) 2-(5-chloro-3-pyridyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (81) 2-(N-(4-fluorobenzamido))-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (82) 2-(N-(cyclohexylcarboxamido))-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (83) 2,4-bis(cyclobutylmethoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (84) 2-cyclobutylmethoxy-4-(6-fluoro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (85) 2-cyclobutylmethoxy-4-(5-chloro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (86) 2-methylsulfonyl-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (87) 2-cyclobutylmethoxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (88) 2-(2,2-dimethylpropyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (89) 2-(2-t-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (90) 2-(2-cyclobutyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (91) 2-(n-propyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (92) 2-(n-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (93) 2-(sec-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (94) 2-(iso-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (95) 2-(isopropyloxy)-4-(3-pyridyloxy)-5-(4-chtorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (96) 2-(n-pentyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (97) 2-cyclopropyloxy-4-(4-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (98) 2,4-bis-(4-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (99) 2-(isobutyloxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (100) 2-(cyclopropylmethoxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (101) 2-(isopropyloxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (102) 2-ethoxy-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (103) 2-(N-pyrrolidinyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (104) 2-(N,N',N'-trimethyl-ethylenediamino)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (105) 2-(N-piperidinyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (106) 2-(N-morpholinyl)-ethylenediamino-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (107) 2-dimethylamino-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (108) 2-(N-pyrrolidinyl)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (109) 2-methylsulfonyi-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (110) 2-(2-isopropyloxy)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (111) 2-(2-N,N',N'-trimethyl-ethylenediamino)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (112) 2-(2-pyrrolidinyl)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (113) 2-(methylsulfonyl)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (114) 2-methoxy-4-(methylsulfonyi)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (115) 2-(3,4-difluorophenyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (116) 2-methoxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (117) 2-(3-fluorophenyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (118) 2-methoxy-4-(3-fluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (119) 2-methoxy-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (120) 2-(2-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (121) 2-(5-chloro-3-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (122) 2-methoxy-4-(5-chloro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (123) 2-(3-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (124) 2-methoxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (125) 2-methoxy-4-(4-fluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (126) 2-methoxy-4-(3,5-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (127) 2-methoxy-4-(3-cyanophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (128) 2-(3,4-difluorobenzyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (129) 2-methoxy-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (130) 2-(methylsulfonyl)-4-ethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (131) 2-ethoxy-4-(methylsulfonyl)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (132) 2-(3,4-difluorobenzyloxy)-4-ethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (133) 2-ethoxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (134) 2-(methylsulfonyl)-4-isopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;

- (135) 2-isopropyloxy-4-(methylsulfonyl)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (136) 2-(3,4-difluorobenzyloxy)-4-isopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (137) 2-isopropyloxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (138) 2-(3,4-difluorobenzyloxy)-4-pyrrolidinyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (139) 2-(3,4-difluorobenzyloxy)-4-dicthylamino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (140) 2-(3,4-difluorobenzyloxy)-4-dimethylamino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (141) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-fluorophenyl)-6-[2, 4-dichlorophenyl]pyrimidine;
- (142) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-methoxyphenyl)-6-[2, 4-dichlorophenyl]pyrimidine;
- (143) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-trifluoromethylphenyl)-6-[2, 4-dichlorophenyl] pyrimidine;
- (144) 2-(3,4-difluorophenoxy)-4-methoxy-5-(3-chlorophenyl)-6-[2, 4-dichlorophenyl]pyrimidine; and
- (145) 2-(3,4-difluorophenoxy)-4-methoxy-5-(3-methoxyphenyl)-6-[2, 4-dichlorophenyl]pyrimidine, or a pharmaceutically acceptable salt thereof.

Claim 27 (new) The method according to Claim 11, wherein in the compound of structural formula I,

R1 is selected from:

- (1) C<sub>1-6</sub>alkyl,
- (2) -QH,
- OC1-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (4) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (5) cycloalkyl-C<sub>1-4</sub>alkyloxy-, unsubstituted or substituted with one to three RC substituents.
- (6) cycloheteroalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (7) cycloheteroalkyl-C<sub>1-4</sub> alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (8) phenyloxy, unsubstituted or substituted with one to three Rc substituents,
- (9) heteroaryloxy, unsubstituted or substituted with one to three RC substituents,
- (10) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (11) heteroaryl-C<sub>1</sub>-4alkyloxy, unsubstituted or substituted with one to three R<sup>c</sup> substituents,

- (12) -NRaRb,
- (13) -NRbC(O)Ra,
- (14) -CO<sub>2</sub>H,
- (15) C<sub>1-6</sub>alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (16) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents.
- (17) cycloalkyl-C<sub>1</sub>-4alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (19) heteroaryloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) phenyl-C<sub>1</sub>-4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (21) heteroaryl-C<sub>1</sub>-4alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>C</sup> substituents,
- (22) -C(O)NRaRb,
- (23) cyano,
- (24) -SO<sub>2</sub>C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents; and provided that R<sup>1</sup> is not -NH<sub>2</sub>;

or a pharmaceutically acceptable salt thereof.

Claim 28. (new) The method according to Claim 27, wherein, in the compound of structural formula I:

Ra and Rb are each selected from:

- (1) hydrogen,
- (2) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (3) cycloalkyl, unsubstituted or substituted with one to three Rc substituents,
- (4) cycloalkyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents,
- (5) phenyl, unsubstituted or substituted with one to three Rc substituents,
- (6) heteroaryl, unsubstituted or substituted with one to three Rc substituents,
- (7) phenyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents, or
- (8) heteroaryl-C<sub>1</sub>-4alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or when bonded to nitrogen, R<sup>a</sup> and R<sup>b</sup> together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R<sup>d</sup>, unsubstituted or substituted on carbon with one to three R<sup>c</sup> substitutents:

or a pharmaceutically acceptable salts thereof.

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Claim 29. (new) The method according to Claim 28, wherein, in the compound according to Claim 1.

## R1 is selected from:

- (1) C<sub>1-6</sub>alkyl,
- (2) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (3) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two Rc substituents,
- (4) cycloalkyl-C1-3alkyloxy-, unsubstituted or substituted with one to two RC substituents,
- (5) phenyloxy, unsubstituted or substituted with one to two RC substituents.
- (6) pyridyloxy, unsubstituted or substituted with one to two RC substituents,
- (7) phenyl-C<sub>1-3</sub>alkyloxy, unsubstituted or substituted with one to two R<sup>c</sup> substituents,
- (8) pyridyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
- (9) -NRaRb, wherein:

### Ra is selected from:

- (a) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents.
- (b) cycloalkyl, unsubstituted or substituted with one to two RC substituents,
- (c) cycloalkyl-C1\_4alkyl, unsubstituted or substituted with one to two RC substituents,
- (d) phenyl, unsubstituted or substituted with one to two Rc substituents.
- heteroaryl, unsubstituted or substituted with one to two RC substituents, (e)
- benzyl, unsubstituted or substituted with one to two RC substituents, (f)R<sup>b</sup> is selected from:
- (a) hydrogen,
- C1-6alkyl, unsubstituted or substituted with one to three Rc substituents, or Ra and Rb together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to two Rc substitutents,

## (10) -NRbC(O)Ra, wherein:

## Ra is selected from:

- (a) hydrogen.
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- cycloalkyl, unsubstituted or substituted with one to two Rc substituents, (c)
- (d) cycloalkyl-C1\_4alkyl, unsubstituted or substituted with one to two Rc substituents,
- (c) phenyl, unsubstituted or substituted with one to two RC substituents,

- (f) pyridyl, unsubstituted or substituted with one to three Rc substituents,
- (g) benzyl, unsubstituted or substituted with one to two Rc substituents.
- (h) pyridylmethyl-, unsubstituted or substituted with one to three Rc substituents,

# Rb is selected from:

- (a) hydrogen,
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (11) -CO<sub>2</sub>H,
- (12) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (13) -C(O)NRaRb, wherein;

Ra is selected from:

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,

Rb is selected from:

- (a) hydrogen, and
- (b) C<sub>1-6</sub>alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents.
- (14) cyano
- (15) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (16) -SO<sub>2</sub>C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents; each R<sup>c</sup> is independently selected from:
  - (1) C<sub>1-3</sub>alkyl,
  - (2) hydroxy,
  - (3) -OC1-3alkyl,
  - (4) halogen,
  - (5) -SCH3,
  - (6) -SH,
  - (7) -NRdRe
  - (8)  $-C(O)C_{1-3}$ alkyi
  - (9) -CO2C1-3alkyl,
  - (10) -CO<sub>2</sub>H,
  - (11) -CN,
  - (12) -CF<sub>3</sub>,
  - (13) -OCF3,
  - (14) cycloheteroalkyl,
  - (15) phenyl,
  - (16) benzyl, and
  - (17) pyridyl;

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### or a pharmaceutically acceptable salts thereof.

Claim 30. (new) The method according to Claim 28, wherein, in the compound according to Claim 1, R<sup>2</sup> is selected from:

- (1) hydrogen,
- (2) C<sub>1-6</sub>alkyl,
- (3) -OH.
- (4) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (5) cycloalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (6) cycloalkyl-C1\_4alkyloxy-, unsubstituted or substituted with one to three RC substituents.
- (7) cycloheteroalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (8) cycloheteroalkyl-C<sub>1-4</sub> alkyloxy, unsubstituted or substituted with one to three Rc substituents,
- (9) phenyloxy, unsubstituted or substituted with one to three Rc substituents,
- (10) heteroaryloxy, unsubstituted or substituted with one to three RC substituents,
- (11) phenyl-C1\_4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (12) heteroaryl-C1-4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (13) -NRaRb.
- (14) -NRbC(O)Ra,
- (15) -CO<sub>2</sub>H,
- (16) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (18) cycloalkyl-C<sub>1-4</sub>alkyloxycarbonyl-, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (19) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) heteroaryloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (21) phenyl-C<sub>1-4</sub>alkyloxycarbonyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents,
- (22) heteroaryl-C<sub>1</sub>-4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (23) -C(O)NRaRb,
- (24) cyano,
- (25) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (26) -SO<sub>2</sub>C<sub>1</sub>-6alkyl, unsubstituted or substituted with one to three R<sup>c</sup> substituents, or a pharmaceutically acceptable salts thereof.

Claim 31. (new) The method according to Claim 27, wherein, in the compound of formula I: R1 is selected from:

- (1) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- (2) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (3) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (4) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (5) 4-fluorophenyloxy, 4-chlorophenyloxy, 4-methoxyphenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy,
- (6) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (7) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-dichlorobenzyloxy, 2,4-fluorobenzyloxy, 2,4-dichlorobenzyloxy, alpha-methyl-4-fluorobenzyloxy, or alpha,alpha-dimethyl-4-chlorobenzyloxy,
- (8) 2-pyridylmethyloxy 3,-pyridylmethyloxy, or 4-pyridylmethyloxy,
- (9) N-methylamino, N,N-dimethyamino, N,N-diisopropylamino, or N(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, or N-containing heterocycloalkyl bonded via nitrogen selected from: morpholinyl, thiomorpholinyl, pyrrotidinyl, piperidinyl, and [2.2.1]azabicycloheptyl,
- (10) -NHCORa wherein Ra is selected from:
  - (a) hydrogen,
  - (b) C<sub>1-4</sub>alkyl,
  - (c) C4-6cycloalkyl, and
  - (d) phenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, or 3,4-dichlorophenyl,
- (11) -CO<sub>2</sub>H,
- (12)  $-C(O)NH_2$ ,
- (13) -CN, and
- (14) -SO<sub>2</sub>CH<sub>3</sub>:

#### R<sup>2</sup> is selected from:

- (1) hydrogen,
- (2) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,

- (3) –OH,
- (4) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (5) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (6) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (7) 4-fluorophenyloxy, 4-chlorophenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3-cyanophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, or phenyloxy,
- (8) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-dichlorobenzyloxy, 2,4-fluorobenzyloxy, or 2,4-dichlorobenzyloxy,
- (9) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (10) amino, N-methylamino, N-cthylamino, N,N-dimethyamino, N,N-diethylamino,N,N-diisopropylamino, or N-containing heterocycloalkyl bonded via nitrogen selected from: pyrrolidinyl, and piperidinyl,
- (11) -NHCORa wherein Ra is selected from:
  - (a) hydrogen, and
  - (b) C<sub>1-4</sub>alkyl,
- (12) -CN, and
- (13) -SO<sub>2</sub>CH<sub>3</sub>;

R3 and R4 are each independently selected from:

- (1) 4-chlorophenyl,
- (2) 4-methoxyphenyl,
- (3) 4-fluorophenyl.
- (4) 4-trifluoromethylphenyl,
- (5) 3-chlorophenyi,
- (6) 3-methoxyphenyl,
- (7) 2,4-dichlorophenyl, and
- (8) 2-chloro-4-methylthiophenyl;

or a pharmaceutically acceptable salts thereof.

Claim 32. (new) The method according to Claim 31, wherein, in the compound of formula I: R3 is 4-chlorophenyl and R4 is 2,4-dichlorophenyl, or a pharmaceutically acceptable salt thereof.